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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,960	05/09/2005	Bill Clark	PN0222	7113

36335 7590 05/11/2009

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EXAMINER	
KILPATRICK, BRYAN T	

ART UNIT	PAPER NUMBER
1797	

MAIL DATE	DELIVERY MODE
05/11/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,960	CLARK ET AL.	
	Examiner	Art Unit	
	BRYAN T. KILPATRICK	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *2-5,9-24 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-8,25 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. The amendments filed on 02 February 2009 have been received and fully considered.

2. Applicant has amended claims 1, 25, and 27; and has canceled claims 4-5, 24, and 26.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Objections

Claim 1 is objected to because of the following informalities: in the second line of section e), the word “ware” is after “which,” it appears that the word "are" should be there instead. Appropriate correction is required.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140

F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed **terminal disclaimer** in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 6-8, 25, and 27 are provisionally rejected on the ground of nonstatutory double patenting over claims 1-3 and 10-16 of copending Application No. 10/512,009 – U. S. Patent Application Publication 2005/0232864 (CLARK et al.). This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows:

Instant claim 1 recites a method of determining *in vivo* protein activity comprised of hyperpolarizing via DNP NMR active nuclei of samples collected from humans or non-humans pre-administered with at least two probe compounds containing at least one NMR active nuclei, and analyzing the samples by NMR spectroscopy. Claims 1-3 and 11 of CLARK et al. recite a method of phenotyping comprised of determining *in vivo* protein activity by hyperpolarizing (wherein the hyperpolarizing step is carried out by one of means of polarization transfer from a noble gas, brute force, dynamic nuclear

polarization (DNP), and spin refrigeration) the NMR active nuclei of samples collected from a human pre-administered with at least one probe compound were at least one probe compound contains at least one NMR active nuclei, and analyzing the samples by NMR spectroscopy. Instant claim 6 sates the collected samples are biofluids, claim 12 of CLARK et al. states the same limitation. Instant claim 7 states the probe compounds are substrates, inducers, or inhibitors for Cytochrome P450 (CYP450); this limitation is met by claim 14 of CLARK et al. Instant claim 8 states CYP1A2, CYP2A6, CYP2C8/9, CYP2C19, CYP2D6, CYP2E1 and CYP3A4; this limitation is met by claim 15 of CLARK et al. Instant claims 25 and 27 state a list of proteins and probe compounds used for determining protein activity; claims 13 and 16 of CLARK et al. state the same proteins and compounds for determining protein activity, respectively.

Furthermore, there is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending application. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 6 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over W. O. 00/40988 (ARDENKJAER-LARSEN et al.).

Instant claim 1 recites a method of determining *in vivo* protein activity comprised of: a.) hyperpolarizing by dynamic nuclear polarization (DNP) the NMR active nuclei of samples collected from humans or non-humans pre-administered with at least two probe compounds containing at least one of C^{13} and N^{15} NMR active nuclei; b.) analyzing sample by NMR to generate an NMR pattern; c.) hyperpolarizing NMR active nuclei of samples collected from humans or non-humans with at least two probe compounds and at least one putative drug; d.) analyzing the samples after drug interaction; and then e.) comparing the samples by NMR spectroscopy to identify protein activity caused by the putative drug. ARDENKJAER-LARSEN et al. discloses an *in vitro* assay method comprised of using an assay reagent containing at least one NMR active nucleus to perform an assay; hyperpolarizing at least one NMR active nucleus of the assay reagent; analyzing the assay reagent and/or assay (similar to a sample) by NMR; and optionally using NMR data to generate assay results (page 3, lines 16-23). The prior art discloses that the NMR active nuclei include C^{13} and N^{15} in line 26 of page 3. Lines 9-18 of page 5 disclose the analysis of an assay and/or assay agent analyzed before and after hyperpolarizing for comparing. The prior art further discloses several biological assays for implementing the disclosed method in lines 13-28 of page 7, a method of polarization comprised of DNP (line 29, page 12–line 11, page 13), and the use of multiple hyperpolarizable probes in line 26 of page 15.

ARDENKJAER-LARSEN et al. discloses an *in vitro* assay method in line 16 of page 3. However, the prior art discloses that the changes observed by the assay can be observed both *in vivo* and *in vitro* in line 8 of page 4.

Instant claim 6 recites the sample to be bio-fluids. ARDENKJAER-LARSEN et al. discloses assay methods covered by the prior art are related to biological macromolecules in line 10 of page 4.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 7-8, 25, and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over W. O. 00/40988 (ARDENKJAER-LARSEN et al.) as applied to claims 1 and 6 above.

Instant claim 7 recites the probe compounds are substrates, inducers, or inhibitors for Cytochrome P450 (CYP450). Instant claim 8 recites the probe compounds are substrates, inducers, or inhibitors for Cytochrome P450 (CYP450) are chosen from CYP1A2, CYP2A6, CYP2C8/9, CYP2C19, CYP2D6, CYP2E1 and CYP3A4. Instant claim 25 requires the probe compounds to be substrates, inducers, or inhibitors of proteins selected from a group disclosed in the current instant claim. Instant claim 27 requires that the probe compounds be selected from a group listed in the current instant claim. ARDENKJAER-LARSEN et al. teaches that biological species is one that is present in living systems, or that is introduced into and is reactive with such systems in lines 8-9 of page 4. The prior art also teaches an assay method for analyzing biological macromolecules such as proteins such as enzymes, receptors, DNA, RNA binding proteins, and carrier proteins (similar to cytochrome); olignucleotides such as DNA and RNA probes; macrocyclic molecules such as cyclodextrin; carbohydrate

macromolecules; and lipids (page 4, lines 10-13). The prior art further teaches assays encompassed by the disclosed method such as enzyme-substrate inhibitors, nuclease assays, etc. (page 7, lines 13-19).

ARDENKJAER-LARSEN et al. does not explicitly disclose the compounds recited in instant claims 7-8, 25, and 27. However, the description of "biological species" taught by the prior art describes the compounds recited by the instant claims. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use compounds as biological species for the purpose of observing physical or chemical changes as disclosed in lines 6-7 of page 4.

Response to Arguments

Applicant's arguments with respect to claims 1, 6-8, 25, and 27 have been considered but are moot in view of the new ground(s) of rejection necessitated by Applicant's amendments to the instant claims.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. W. O. 99/35508 (ARDENKJAER-LARSEN et al.) and U. S. Patent 6,278,893 (ARDENKJAER-LARSEN et al.) both disclose methods of magnetic resonance for investigating human or non-human samples using polarization in their respective Abstracts.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BRYAN T. KILPATRICK whose telephone number is (571)270-5553. The examiner can normally be reached on Monday - Friday, 7:30 am - 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (571)272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Samuel P Siefke/
Primary Examiner, Art Unit 1797

BK
AU 4112/1797